

of scaffold; or in an amount from about 0.1 to about 5000 $\mu\text{g/ml}$ of scaffold; or in an amount from about 1 to about 5000 $\mu\text{g/ml}$ of scaffold.

[0023] Additional embodiments of the present invention include compositions that comprises materials of the scaffolds described herein. One aspect is a composition that comprises at least one polyisocyanate, polyisocyanate prepolymer, or both; at least one polyester polyol; at least one catalyst; and at least one biologically active component in powder form. The biological agents are described above.

[0024] Additional embodiments include methods of using the compositions and scaffolds of the present invention. One example is their use in a method of delivering a biologically active agent to a wound site. This example can comprise providing a composition that comprises at least one polyisocyanate, polyisocyanate prepolymer, or both; at least one polyester polyol; at least one catalyst; and at least one biologically active component in powder form; and contacting the composition with a wound site. The wound site may be, for example, part of a bone or skin.

[0025] Other embodiments will be apparent from a reading of the disclosure.

BRIEF DESCRIPTION OF THE DRAWINGS

[0026] FIG. 1 shows an example of the delivery of an embodiment of the present invention.

[0027] FIG. 2 is a graph showing tobramycin release kinetics.

[0028] FIG. 3 shows a rat wound healing model.

[0029] FIG. 4 is graph showing tobramycin release.

[0030] FIG. 5 shows in vivo response to foam in a rat excisional dermal wound.

[0031] FIG. 6 is a scanning electron micrograph (SEM) of T6C3G1L-PEG0 scaffold.

[0032] FIG. 7 shows in vitro tobramycin release from PUR scaffolds and PMMA beads. Materials were incubated at 37° C. in PBS, which was completely removed and refreshed at each time point. Tobramycin concentration in the releasate was measured by HPLC.

[0033] FIG. 8 shows zones of inhibition (ZI) measured after 24 hours for PUR scaffolds using the Kirby-Bauer test. PMMA control: ~6-mm PMMA beads with 4.0 wt-% tobramycin. Positive control: 10- μg tobramycin BBL SensiDiscs. Negative control: PUR scaffolds with no tobramycin. Asterisks denote statistical significance ($p < 0.005$) with respect to the positive control and PMMA.

[0034] FIG. 9 shows bioactivity of tobramycin released from PUR scaffolds after 8, 20, and 30 days of incubation in PBS, evaluated by Kirby-Bauer tests. Blank BBL SensiDiscs were loaded with 0.5 μg tobramycin (in 10 μL) PBS) from each releasate (as determined by HPLC), as well as 0.5 μg exogenous tobramycin for the positive control. Asterisks denote statistical significance ($p < 0.005$) with respect to the positive control.

[0035] FIG. 10 shows storage (bold) and loss moduli as a function of shear rate in compression mode during DMA frequency sweeps from 0.1 to 10 Hz. Illustrated are the results from T6C3G1L scaffolds with 0%, 30%, and 50% PEG, each with (solid line) and without (dotted line) tobramycin.

[0036] FIG. 11 shows DMA stress relaxation response to 2% strain (compression) over 20 minutes of PUR scaffolds with 0%, 30%, and 50% PEG, with (solid line) and without (dotted line) tobramycin.

[0037] FIG. 12 is a chart that shows in vitro release profile of BSA-FITC from PUR scaffold. BSA-FITC was included into the scaffold as solution in presence of 0.5% glucose, and as powder in presence of different weight percentage of glucose.

[0038] FIG. 13 is a chart that shows in vitro release profile of PDGF-BB from PUR scaffold including PDGF-BB powder (PUR-PDGF). Also included are 0.05% heparin and 2% glucose, and the release kinetics was determined by Iodine125 labeling and ELISA respectively.

[0039] FIG. 14 is a chart that shows in vitro release profile of PDGF-BB from PLGA particles, granules and polyurethane scaffold containing granules (PUR-Granules). The release kinetics was determined by Iodine125 labeling (A) and ELISA (B) respectively.

[0040] FIG. 15 is a chart that shows in vitro cell proliferation ability of PDGF-BB releasates from PUR-PDGF (A), Particles (B), Granules (C), and PUR-Granules (D) respectively.

[0041] FIG. 16 is scanning electronic microscopic images of polyurethane scaffold containing 2% glucose (A), and containing 15% granules (B).

[0042] FIG. 17 is scanning electronic microscopic images of polyurethane scaffold containing 80 μm PLGA particles (A), and 1 μm PLGA particles (B).

[0043] FIG. 18 shows data in connection with the release of BSA-FITC from PUR scaffolds.

[0044] FIG. 19 shows data in connection with the release of BMP-2 from PUR scaffolds.

[0045] FIG. 20 shows the results of an ALP assay of BMP-2 releasate liquids.

DESCRIPTION OF THE INVENTION

[0046] Aspects of the present invention include injectable, biodegradable poly(ester urethane)urea (PEUUR) foams for use as scaffolds and delivery systems for bioactive agents to promote fracture healing and bone regeneration.

[0047] An example of the foam scaffold may be made by reactive liquid molding of two components: an aliphatic isocyanate and a resin composed of a poly(ϵ -caprolactone-co-glycolide-co-lactide) polyol, water, triethylenediamine catalyst, sulfated castor oil stabilizer, and calcium stearate pore opener. As shown in FIG. 1, an advantage of these materials is that the degradation rate of the scaffold and the bioactive release kinetics can be controlled independently. In addition to providing structural support for healing bone, the scaffolds can locally release bioactive agents to the fracture site at a controlled rate. Such bioactive agents include small molecules (e.g., antibiotics and statins) and proteins, such as bone morphogenetic protein-2 (BMP-2) and platelet-derived growth factor (PDGF). The antibiotics, such as tobramycin, serve to fight infections that can hinder the healing process. Statins have been shown to enhance bone healing by upregulating BMP-2 expression.

[0048] Another example of a scaffold of the present invention is a scaffold of Patent Application Publication Number 2007/299151, incorporated herein by reference. Accordingly, an embodiment of the present invention is a scaffold synthesized from the steps of: coating a biodegradable and bioactive polyurethane polymer with human osteoblastic precursor cells, the polymer being synthesized by reacting isocyanate groups of at least one multifunctional isocyanate compound with at least one bioactive agent having at least one reactive group —X which is a hydroxyl group (—OH) or an amine